REMARKS/DISCUSSION OF ISSUES

This response is intended as a full and complete response to the non-final Office Action mailed February 24, 2004. Claims 1-111 are currently pending. Claims 1-24 and 99-111 are rejected and claims 25-98 have been withdrawn from consideration. As explained below, all of the rejected claims are patentable.

I. REJECTIONS UNDER 35 USC §101

Claims 1-24 and 99-111 stand rejected under 35 USC §101. Independent claims 1, 12, 23, 99, 105 and 107 have been amended to address the rejection and are believed to be directed to statutory subject matter under the provisions of 35 USC §101. Specifically, Applicants' claims recite methods for evaluating at least one metabolic pathway. In doing so, Applicants claim the ability to identify a set of substrates and/or reactant-product relationships that will be sufficient to produce a set of products. Alternatively, Applicants also claim the ability to identify a set of substrates and/or reactant-product relationships that will be insufficient to produce a set of products. The ability to identify such substrates and/or reactant-product relationships and products in the context of evaluating a metabolic pathway produces a useful, concrete and tangible results. Therefore, Applicants submit that claims 1-24 and 99-111 fully satisfy the requirements of 35 USC §101 and are patentable thereunder.

II. REJECTIONS UNDER 35 USC §112, SECOND PARAGRAPH

Claims 2, 5, 6, 10 and 21 are rejected under 35 U.S.C. 112, second paragraph. Responsive to the Examiner, claims 2, 5, 6, and 21 have been amended to address the present rejection.

However, Applicants decline to amend claim 10 because claim 10 is definite. Applicants recite the limitation of "least cost path" and this limitation is clearly supported in Applicants' specification, e.g., page 36, lines 1-19. Applicants stated in the specification that the costs can be assigned based on real-world practicality. Thus, it can be based on distance and/or energy as indicated by the Examiner. Applicants

submit that claims 2, 5, 6, 10 and 21 fully satisfy the requirements of 35 USC §112, second paragraph and are patentable thereunder.

III. REJECTIONS UNDER 35 USC §102(b)

Claims 1-18, 20-24, 99-107 and 109-111 stand rejected under 35 USC §102(b) as being anticipated by Akutsu et al (*Bioinformatics*, Vol. 16, No. 8 (2000), pages 727-734). Applicants respectfully disagree.

Akutsu describes a qualitative network model which is an intermediate model between the Boolean network model and the differential equation model. The model can be considered as a combination of the Boolean network and qualitative reasoning model. In this model, regulation rules are represented as qualitative rules and embedded in network structures. (See Akutsu, Page 727, column 2). Akutsu states that the qualitative networks are used not for simulation but to represent biological knowledge. Akutsu further states that one does not need to know precise values of values but one needs to know topologies of networks. Akutsu states that the exact fitting of parameters does not seem to be realistic because it is very difficult to make precise quantitative models of complex biological networks (See Akutsu, Page 729, column 1).

Akutsu then states that the proposed methods are difficult to be applied to real data because (1) the regulation rules of genes may be much more complex than linear differential equations and S-systems, (2) the formalism using differential equations implicitly assumes that concentration of transcription factors can be observed, but is much more difficult to monitor the concentration of proteins and there may be a long delay of hours between mRNA and protein, (3) the proposed methods for differential equations are not robust for noises, (4) the proposed methods are not fast enough for handling many genes (See Akutsu, Page 733, column 1).

In contrast with Akutsu, Applicants' claims 1, 12, 23 and 99, 105, 106 and 107 are directed to or include the limitation of a symbolic model for evaluating a metabolic pathway which is represented by a Boolean function. To illustrate, as stated in Claim 1, a method is provided having a model that represents a network of chemical reactions that express a relationship between the pathway components. At least some of the

elements represent pathway components comprising a set of precursor substrates, and at least some of the elements represent pathway components comprising a set of target products. The symbolic model is evaluated to identify a set of precursor substrates and/or chemical reactions that is sufficient to produce a set of target products or to identify a set of precursor substrates and/or chemical reactions that is insufficient to produce a set of target products. This novel use of the symbolic model is completely absent in the Akutsu reference.

Therefore, Akutsu does not teach or suggest the limitations of claims 1, 12, 23, 99, 105, 106 and 107. In fact, by teaching that the proposed qualitative networks are not used for simulation but to represent biological knowledge and that the exact fitting of parameters does not seem to be realistic because it is very difficult to make precise quantitative models of complex biological networks, Akutsu teaches away from Applicants' invention.

Applicants submit that claims 1, 12, 23, 99, 105, 106 and 107 and all claims that depend therefrom are not anticipated by Akutsu. Therefore, claims 1-18, 20-24, 99-107 and 109-111 are allowable and withdrawal of the 35 U.S.C. §102(b) rejection is respectfully requested.

CONCLUSION

Applicants submit that all claims now pending are in condition for allowance. Accordingly, both reconsideration of this application and its swift passage to issuance are earnestly solicited.

If, however, the Examiner believes that any unresolved issues still exist, it is requested that the Examiner telephone the undersigned at (732) 530-9404 so that appropriate arrangements can be made for resolving such issues as expeditiously as possible.

Respectfully submitted,

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